

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Helke Hillebrand et al.

Application No.: 10/593,181

Confirmation No.: 6326

Filed: September 15, 2006

Art Unit: 1638

For: IMPROVED CONSTRUCTS FOR MARKER
EXCISION BASED ON DUAL-FUNCTION
SELECTION MARKER

Examiner: C. K. Worley

MS Appeal Brief – Patents
Commissioner for Patents
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APPELLANTS' REPLY BRIEF

In response to the Examiner's Answer, dated July 21, 2010, in the above-referenced application on appeal ("the Answer"), Appellants submit herewith a Reply Brief. This Reply Brief is being timely filed, within two months of the mailing date of the Answer, on or before September 21, 2010.

Appellants respectfully request that the Board of Patent Appeals and Interferences, before making its decision on this appeal, consider the following rebuttal to statements made in the Answer, as set forth below in detail.

REMARKS

Appellants respectfully disagree with the Examiner's arguments and contentions advanced in the Answer concerning the rejections of claims 1-4, 10, and 27 under 35 U.S.C. 103(a) as allegedly obvious over Signer *et al.* WO 01/96583 ("Signer") in view of Nasholm *et al.* WO 03/060133 ('Nasholm') "and taken with the evidence of Stougaard" *et al.* ('Stougaard') "and the evidence of Boeke *et al.*" ('Boeke') for at least those reasons originally set forth in Appellants' Brief on Appeal. In this Reply Brief, Appellants highlight for the Honorable Board the specific items from the Answer which Appellants feel are most errant.

The Examiner's Answer advances two general rejoinders to Appellants' arguments on appeal. Appellants' reply to each general rejoinder of the Examiner is set forth below:

1) The Answer at page 6 and at page 8 argues that the secondary references Nasholm and Stougaard allegedly teach that a single transgene "could be useful as both a positive and a negative selection marker" and as such it would be obvious to modify Signer to utilize a construct encoding a D-amino acid oxidase. Appellants strongly disagree.

In reply, rather Stougaard teach that *CodA* can be used as either a negative selectable marker or a positive selectable marker. Nothing in Stougaard discloses the use of *CodA* as a dual-functional selection marker in one construct. The teachings are similar for D-amino acid oxidase in Nasholm. The Examiner also acknowledges that Nasholm teaches that "D-amino acids can be used as either positive selection or negative selection." (Answer, p. 9, ll. 5-6) (emphasis added).

Moreover, as explained in detail in the Appeal Brief at pages 10-16, the modification to Signer suggested by the Examiner would require a substantial reconstruction and redesign of the construct being modified.

The Answer further alleges that "[t]he fact that the URA 3 gene is used as a positive selection based on auxotrophy . . . instead of being used as a positive selection based on media comprising a toxic compound, is not a relevant fact." (Answer, p. 8, ll. 4-7). However, the entire obviousness rejection rests on Boeke allegedly teaching "the use of one dual function selectable marker (the URA3 gene)." (Answer, p. 8, ll. 1-2). The fact that the alleged positive selection that is ascribed to the URA3 gene cannot be considered a positive selection as claimed is clearly relevant. Boeke only discloses one selection medium comprising one compound (*i.e.* 5-FOA) which can act on a selectable marker. The

interpretation that Boeke teaches one dual function selectable marker is in error and as such the basis for the rejection is untenable. Reversal of the rejection is respectfully urged.

2) The Answer at pages 7-10 further argues that "Appellant's arguments are an attack on the references individually rather than considering them as a whole in combination." (Answer, p. 7, ll. 11-12). Appellants strongly disagree.

Explaining the teachings of the primary and secondary references, explaining how the teachings of the secondary references do not remedy the deficiencies of the primary reference, and explaining how the references are not combinable is not an attack on the references individually but rather provide the proper analysis as outlined under *KSR*.

As clearly explained in *KSR* (*KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 1740 (2007)) and *John Deere* (*Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966)), the teachings of the references must first be determined followed by a comparison between the references and the claims to ascertain the differences. Such determinations can only be done initially by evaluating each of the references and how these references differ from the claims. This is what is done in Appellants' briefs.

More specifically, the arguments presented at pages 8-10 of the Appeal Brief explain why the references are not combinable. Contrary to the Examiner's assertion, the combined teachings of the references are being considered and the references are ascertained as not being combinable. Moreover, at page 10 of the Appeal Brief, the combined teaching of the references are clearly being considered when stating that "[e]ven assuming *arguendo* that one skilled in the art would consider combining these four references, they do not disclose . . ."; *i.e.* that the combined teaching of the references do not disclose or suggest all the claim limitations.

In addition, the arguments presented at pages 10-16 of the Appeal Brief in part further explain that the teachings of the references have not been considered as a whole and have been mischaracterized. For example, the basis for the obviousness rejection is premised on Boeke allegedly teaching "the idea of using one marker for both positive and negative selection" (Final Office Action dated December 2, 2009, p. 12, ll. 11-13, p. 15, ll. 19-20, p. 16, ll. 5-7) or as stated in the Answer as teaching "the use of one dual function selectable marker." (Answer, p. 8, ll. 1). Boeke does not stand for this teaching. Rather Boeke only discloses one selection medium comprising one compound which can act on a selectable marker. Additionally, the arguments presented at pages 10-16 explain how the redesigning of the construct of the primary reference suggested by the Examiner would change its basic

principle of operation. Explaining the teachings of the references, how these have been misinterpreted and not viewed as a whole, explaining how they differ from the claimed invention, and explaining how the modification and redesign suggested by the Examiner are counter to the principle under which the construct of Signer was designed to operate rather provide the proper analysis as outlined under *KSR*.

Furthermore, the arguments presented at pages 16-17 of the Appeal Brief explain how even if the references were combined, the combination still does not arrive at the claimed invention. This is clearly not an attack on the references individually.

The Examiner also alleges that Appellants are ignoring the teaching of Boeke (Answer, p. 8, l. 22). Appellants strongly disagree. When Boeke is considered as a whole as required, Boeke only discloses one selection medium comprising one compound which can act on a selectable marker.

Lastly, the arguments presented at pages 17-19 of the Appeal Brief explain how the references teach away from the claimed invention. Again such explanations provide a proper analysis as outlined under *KSR*.

Appellants' reply to the Examiner's Answer as to specific claims 3, 10, and 27 (Answer, p. 9-10) is discussed below:

Claim 10

The Answer alleges that because Stougaard teaches "a gene of interest . . . that is adjacent to the selectable marker gene," "the limitation that the second expression cassette is not localized between the sequences which allow for specific deletion of the first expression cassette is taught by Stougaard." (Answer, p. 9, ll. 13-17). Appellants respectfully disagree.

In reply, the argument presented in the Appeal Brief relating to claim 10 appears to have been misunderstood. Appellants clarify the argument as follows.

The method taught in Signer requires that a very specific configuration of the construct be used for the elimination of the selectable markers to function. In the Signer construct, the direct repeats of the gene of interest themselves are the sequences that allow for the elimination of the selectable marker. Therefore, the specific configuration and positioning of the gene of interest is critical to the functioning of the method of Signer. Changes to the specific configuration of the construct used in Signer would render the method of Signer inoperable and as such modifications to the construct cannot simply be "an obvious design choice" as concluded by the Examiner. (Answer, p. 10, ll. 2-3).

The construct of Signer comprises direct repeats of the gene of interest which flank the two different types of selectable markers, depicted by the general formula: GI-PS-NS-GI or GI-NS-PS-GI, where GI is the gene of interest, PS is the positive selectable marker gene, and NS is the negative selectable marker gene. (Signer, p. 2, ¶¶ [0006]-[0007]). The Answer alleges that this configuration corresponds to the gene of interest being “interrupted by the selectable marker.” (Answer, p. 10, ll. 4-5). However, this characterization is misplaced. The configuration of the construct of Signer is not an interruption of the gene of interest but rather corresponds to “repeats” of the gene of interest, which are required to effectuate the elimination of the selectable marker.

Moreover, whether or not Stougaard teaches a gene of interest “adjacent to the selectable marker gene” is of no consequence, since in the Signer construct, the gene of interest is also adjacent to a selectable marker. Moreover, the Examiner has stated that it is Signer that “was relied upon to teach the specific method steps.” (Final Office Action dated December 2, 2009, p. 15, l. 8). Thus, based on the specific method steps and construct of Signer required for the elimination of the selectable marker, Signer cannot meet the limitation of “at least one second expression cassette suitable for conferring to said plant an agronomically valuable trait, wherein said second expression cassette is not localized between said sequences which allow for specific deletion of said first expression cassette” as required by claim 10, otherwise the method of Signer would be inoperable.

Because the combined teachings of the references do not teach or suggest all the claim limitations and do not arrive at the claimed invention, a *prima facie* case of obviousness has not been established at least as to claim 10. Reversal of this rejection is respectfully urged.

Claims 3 and 27

The Answer alleges that claims 3 and 27 “do not recite any active method steps or materials that are utilized for ‘inducing deletion of said first expression cassette.’” (Answer, p. 10, ll. 11-13). The Examiner further alleges that the act of allowing sufficient time and growth until recombination occurs naturally satisfies the limitation of “inducing.” (Answer, p. 10, ll. 13-16). Applicants strongly disagree.

In reply, the claims do require an active, positive method step of “inducing deletion,” whether or not the means by which the inducement is done is recited in the claims. In contrast, the method of Signer waits for the recombination to occur naturally and by chance before conducting the second selection. Simply waiting for something to occur naturally or by chance is not an active step.

The Answer nevertheless alleges that such passive waiting for the recombination event to occur meets the limitation of the active step of "inducing." Appellants strongly disagree.

In reply, the Answer is arguing the end goal of arriving at a recombination event and not the method by which the goal is achieved. The Federal Circuit has held that the "**knowledge of the goal does not render its achievement obvious.**" *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1352 (Fed. Cir. 2008) (emphasis added).

As an analogy, there is clearly a distinction between the passive waiting and allowing labor to occur naturally and run its course as compared to inducing labor or inducing the birth of a child whether with chemicals or by surgical means. Both are directed to the same goal of child birth; however, the method steps for arriving at such an end goal are unmistakably distinguishable.

Whether or not various means for inducing deletion were known as mentioned by the Answer is of no consequence, an actual active step of "inducing" deletion as claimed is not the same as passively waiting for an event to occur by chance. An actual active step of "inducing" deletion as claimed is not taught or suggested by any of the references cited and is consequently not taught or suggested by the combined teaching of the references cited. Accordingly, a *prima facie* case of obviousness has not been established for at least claims 3 and 27 and as such reversal of this rejection is strongly urged.

CONCLUSION

In view of the arguments set forth above and in Appellants' Brief on Appeal, Appellants submit that all claims on appeal are patentably distinguishable over the combined teaching of the references cited.

Accordingly, Appellants respectfully request that the Honorable Board reverse the Examiner and find for Appellants in this appeal.

Dated: September 21, 2010

Respectfully submitted,

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